ENUMERATIVE STUDIES ON *T. BRUCEI* IN RATS AND GUINEA-PIGS, AND A COMPARISON WITH *T. RHODESIENSE* AND *T. GAMBIENSE*

BY

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(*Received for publication* 8 *February*, 1912)

This investigation was undertaken while I was assistant to Sir Ronald Ross, under the Sir Edwin Durning-Lawrence Research Fund. Already enumerative studies have been conducted by H. B. Fantham and J. G. Thomson in animals infected with *T. rhodesiense* and *T. gambiense* (1910-11), and a comparison was made between these. It was pointed out that *T. rhodesiense* was more virulent than *T. gambiense*, as shown by the fact that rats and guinea-pigs lived a shorter period when infected with the former, and it was also demonstrated that the incubation period was shorter and the period between the heights of the crests shorter in the cases of rats infected with *T. rhodesiense*.

The following table, based on the results of Fantham and Thomson (1910), shows this difference clearly:—

	No. of Rats examined	Incubation period average, in days	Average duration of life	Period between the heights of the crests
T. rhodesiense ...	22	2·9 days	11·3 days	3-4 days
T. gambiense ...	11	4·4 days	13·8 days	4-6 days

It is possible, therefore, apart from morphology, to distinguish *T. rhodesiense* (Stephens and Fantham, 1910) from *T. gambiense* provided a sufficient number of animals, preferably rats and guinea-pigs, are inoculated with both strains. As a matter of fact, however, the morphology in the case of *T. rhodesiense* in rats, as

pointed out by Stephens and Fantham (1910), makes the diagnosis of *T. rhodesiense* very easy indeed.

I now publish four charts of animals infected with *T. brucei*. The method employed has already been described by D. Thomson (1911). It is necessary in the case of heavily-infected animals to dehaemoglobinise the slide, and spread the film over a large area.

By means of a special pipette (D. Thomson, 1911) a count was made regularly every twenty-four hours of the number of parasites per c.mm. of blood, and these daily counts have been represented diagrammatically in the charts accompanying this paper.

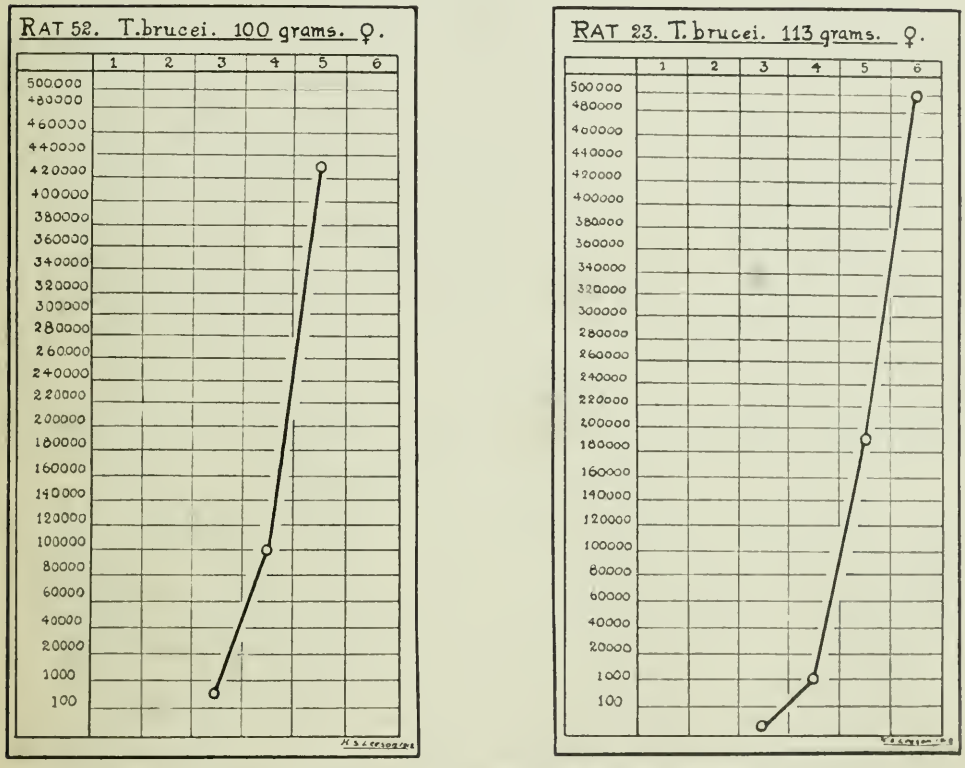
We shall first examine the charts of Rats 52 and 23 (*T. brucei*). Here we note the very rapid multiplication of the parasites. In the case of Rat 52 the parasites rose with a rush from about 1,000 per c.mm. to 430,000 per c.mm. in forty-eight hours, and the animal succumbed. Again, in the case of Rat 23 the parasites rose from under 100 per c.mm. to 490,000 per c.mm. of blood in seventy-two hours, and the animal died shortly after. These extraordinary numbers were never reached in so short a period either in the case of *T. rhodesiense* or *T. gambiense*. In the case of *T. rhodesiense* I have found in a rat treated with atoxyl, and which lived fifty-one days, that the parasites on the fifty-first day rose to one million and a half per c.mm. (R. Ross and J. G. Thomson, 1911), but never in the case of either *T. rhodesiense* or *T. gambiense* have I found the parasites in rats reach such high numbers in forty-eight to seventy-two hours as in the case of *T. brucei*.

Again, it is to be noticed that no periodic variation took place in rats infected with *T. brucei*. The rise was always continuous in the animals observed by me. In the case of rats inoculated with *T. rhodesiense* and *T. gambiense*, H. B. Fantham and J. G. Thomson pointed out that a continuous rise of parasites may take place until death in both (e.g., Rats 18-22, 30-33), but that periodic variation also takes place in both (e.g., Rats 1-17, 23-29). So far, in the strain of *T. brucei* used here, I have been unable to obtain periodic variation in rats, but it is quite possible that such may occur if we could find rats of sufficient resistance.

The rats inoculated with *T. brucei* all died within an average period of six days. When this is compared with the average life of rats inoculated with *T. rhodesiense* and *T. gambiense* we have

a very marked difference. We conclude, therefore, in rats that *T. brucei* is much more virulent than either *T. rhodesiense* or *T. gambiense* as evidenced by three points, namely:—

1. Duration of life.
2. Rapidity of development of parasites.
3. Periodic variations.



GRAPHS SHOW THE DAILY RECORD OF PARASITES FOUND PER CMM. OF PERIPHERAL BLOOD.

Of course *T. brucei* is essentially an animal trypanosome, and so might be expected to be more virulent to rats than strictly human trypanosomes sub-inoculated into them.

We shall now examine the charts of the two guinea-pigs infected with *T. brucei*.

Here again, when we study the disease in *T. rhodesiense* and *T. gambiense*, we find that the disease runs a more or less chronic

course. In the case of *T. rhodesiense* the average life of the guinea-pig was fifty-nine days, whereas those infected with *T. gambiense* was 111 days. The period between the crests of the waves was longer than in rats, namely, five to eight days (H. B. Fantham and J. G. Thomson, 1910).

Referring now to the charts of Guinea-pigs 56 and 67, infected with *T. brucei* (see charts), we find that the longest period of life was twenty-six days, and we find again that in the case of *T. brucei* the multiplication of the parasites was of much greater rapidity than in the case of either *T. rhodesiene* or *T. gambiense*. Thus in the case of Guinea-pig 56 (*T. brucei*) the parasites in eighteen days numbered 450,000 per c.mm., and during that time the rise was more or less continuous. There was only one slight fall during that time, which occurred on the twelfth and thirteenth days. The animal died in twenty days. In the case of Guinea-pig 77 (*T. brucei*) we find that on the eleventh day the parasites rose to about 350,000 per c.mm. and then fell steadily for two days, and no parasites were found on the thirteenth or fourteenth days, and only one or two were seen on a film on the fifteenth day. On the sixteenth day the parasites again reappeared and increased steadily for eleven days until they reached over 500,000 trypanosomes per c.mm. of blood. These numbers far exceed those found in either *T. gambiense* or *T. rhodesiense*. The chart of Guinea-pig 77 is of very great interest, as it shows a distinct periodic variation, with a period of about sixteen days between the heights of the crests. This is interesting because of the fact that it shows on the eleventh day the animal was able to survive a very heavy infection, the crisis being reached and a natural recovery taking place for two days. We had evidently resistant forms left (*cf.* Fantham, 1911).

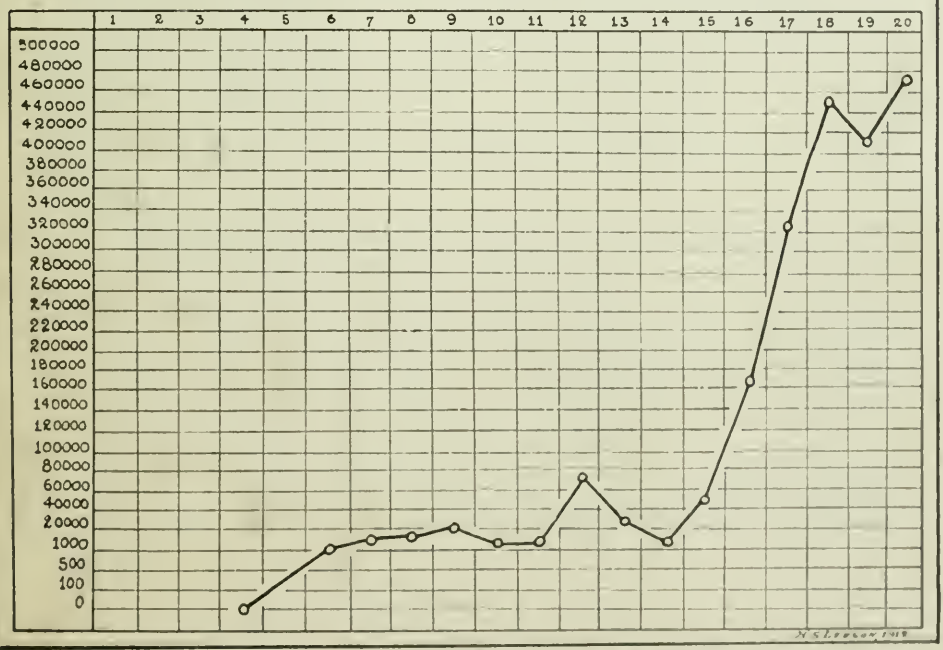
For a permanent cure we must aim at the destruction, therefore, of these resistant forms. In short, if we compare *T. brucei* with *T. rhodesiense* and *T. gambiense* in guinea-pigs we have the following points of difference:—

1. *T. brucei* kills guinea-pigs much more rapidly than *T. rhodesiense* or *T. gambiense*.

2. The multiplication of parasites is much more rapid, and they reach much higher numbers in the peripheral blood than in either *T. rhodesiense* or *T. gambiense*.

GUINEA-PIG 77., ROUGH-HAIRED. *T. BRUCEI*. 474 GRAMS. ♂.

GUINEA-PIG 56., *T. BRUCEI*. 742 GRAMS. ♀.



GRAPHS SHOW THE DAILY RECORD OF PARASITES FOUND PER C.MM. OF PERIPHERAL BLOOD.

3. The periodic variations in *guinea-pigs* infected with *T. brucei* is very different from that which takes place in the case of infections with *T. gambiense* and *T. rhodesiense*.

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